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1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/557,280	WANGH ET AL.	
	Examiner	Art Unit	
	Angela Bertagna	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *24-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23,37 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 November 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-23, 37, and 38 in the reply filed on February 2, 2007 is acknowledged. The traversal is on the ground(s) that search and examination of all of the claims together would not present a serious burden. This argument was not found persuasive, because the instant application is a national stage application filed under 35 U.S.C. 371. As noted in MPEP 803, search and examination burden must be established in restriction requirements made in national applications filed under 35 U.S.C. 111(a). However, for lack of unity requirements made in national stage applications filed under 35 U.S.C. 371, the guidelines set forth in MPEP 1800 are to be followed (see MPEP 801). Chapter 1800 requires that if a special technical feature linking the claims over the prior art is present, the claims must be examined together (see MPEP 1850 and PCT Rule 13.1), but is silent with respect to a requirement to establish an examination burden. Therefore, a discussion of search burden is not required in a lack of unity requirement. As discussed previously, since the prior art of Pourahmadi et al. (US 6,440,725) anticipates the instant claim 24, the claims lack a special technical feature linking them over the prior art. Also, search and examination of all claims together would present a serious burden. A search for the device of Group II would only require a search for the specific structural features of the device and the kit comprising the device and would not require additional search terms directed to methods of using the device, such as the methods of Group I. Since the device of Group II can be used in methods materially different from that of Group I, a search for the method of Group I would not constitute a complete search for the device and kit of Group II. A complete search for the device and kit of Group II would

require additional searching in diverse areas of the prior art materially different from the method of Group I. Therefore, search and examination of all of the claims together cannot be performed without imposing a serious search and examination burden.

The requirement is still deemed proper and is therefore made FINAL.

Claims 24-36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on February 2, 2007.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12-23, 37, and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 12-23, 37, and 38 are indefinite because independent claim 12 recites the phrase "at least about." The phrase "at least about" is indefinite, because the concentration of

chaotropic agent constituting "at least about 2M" is completely unclear. See also MPEP 2173.05(b), which states, "....the court held that claims reciting "at least about" were invalid for indefiniteness where there was close prior art and there was nothing in the specification, prosecution history, or the prior art to provide any indication as to what range of specific activity is covered by the term "about." Amgen, Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991)."

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-9, 12, 13, and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Vodkin et al. (BioTechniques (1994) 17(1): 114-116) as evidenced by Barbeau et al. (US 6,762,160 B2).

The instant claims are drawn to a method of enzymatically processing nucleic acid molecules comprising diluting a mixture of DNA, RNA, degraded or denatured proteins, and a chaotropic agent with an aqueous solution to reduce the concentration of the chaotropic agent to less than 0.01 M and subsequently conducting an enzymatic process, specifically PCR. The enzymatic process occurs without removal of the DNA or RNA from each other or the other components of the mixture.

Vodkin teaches RT-PCR from mosquitoes homogenized in detergent (see abstract).

Regarding claims 1 and 2, Vodkin teaches a method comprising diluting a mixture that includes DNA, RNA, degraded or denatured proteins, and a chaotropic agent with an aqueous reagent to reduce the concentration of the chaotropic agent to less than 0.05 M and subjecting at least some of the DNA and RNA molecules to an enzymatic process without separating them from each other or the other components of the reaction mixture (see page 114, columns 2-3, "Sample Preparation" and "RT-PCR assay" sections). Here, Vodkin teaches that mosquitoes were solubilized in a solution of 50 mM Tris-Cl, pH 7.4, 5 mM EDTA, and 1% SDS. The resulting homogenate includes a mixture of DNA, RNA, degraded or denatured proteins, and a chaotropic agent (SDS). SDS is a chaotropic agent, because it solubilizes membranes, and thereby, disrupts hyrdrophobic interactions. The fact that SDS is a chaotropic agent is also evidenced by the teachings of Barbeau et al. (US 6,762,160 B2 – see column 9, lines 58-64). Also, a 1% solution of SDS corresponds to a concentration of approximately 0.03 M, since the molecular weight of SDS is 288.38 g/mol. Therefore, upon 10-fold or 100-fold dilution with water, the concentration of the chaotropic agent is reduced to 0.003 M or 0.0003 M, which is less than 0.05 M and less than 0.01 M. Vodkin then teaches that an aliquot of the diluted mixture was used without further purification (i.e. without separation of the components of the diluted reaction mixture from one another) in an enzymatic process, specifically RT-PCR (page 114, columns 2-3, "RT-PCR assay").

Regarding claim 3, Vodkin teaches that the mixture includes a cell-lysing detergent (SDS), a water-miscible solvent (water), a chelating agent (EDTA), and a neutralizing buffer (Tris-Cl at pH 7.4) (see page 114, column 2, "Sample Preparation" section).

Regarding claim 4, Vodkin teaches that dilution is accomplished by serial addition of at least two aqueous reagents (see page 114, columns 2-3, where the first dilution is accomplished by adding water, and the second dilution occurs when the resulting aliquot is diluted into the RT reaction buffer).

Regarding claims 5-7, the enzymatic process taught by Vodkin is RT-PCR (page 114, columns 2-3). This is an exponential amplification process that includes a polymerase chain reaction and reverse transcription.

Regarding claims 8 and 9, Vodkin teaches that an enzyme for performing the enzymatic process, and specifically reverse transcriptase, is included in the at least one aqueous reagent (see page 114, columns 2-3, "RT-PCR assay", where the RT is present in the second aqueous dilution reagent).

Regarding claim 12, Vodkin teaches that the mixture is prepared by incubating a sample containing protein-bound RNA and DNA molecules and a chaotropic-agent containing disruption reagent at a concentration of chaotropic agent of at least about 2 M (see page 114, column 2 "Sample Preparation" section, where mosquitoes were homogenized in a buffer containing the chaotropic agent SDS at a concentration of 1%). As noted above in section 2, the phrase "at least about 2 M" is completely unclear as to the minimum concentration of chaotropic agent required, and therefore, the teachings of Vodkin anticipate claim 12.

Regarding claim 13, Vodkin teaches that the incubation of the sample and disruption reagent includes heating, whereby the chaotropic agent is concentrated (see page 114, column 2, "Sample Preparation" section, where Vodkin teaches heating at 94°C for 5 minutes).

Regarding claim 37, Vodkin teaches that incubating and dilution occur in the same container (see page 114, column 2, "Sample Preparation" section).

5. Claims 1-6, 8-13, and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Thornhill et al. (Prenatal Diagnosis (2001) 21: 490-497) as evidenced by Builder et al. (US 5,407,810) and Barbeau et al. (US 6,762,160 B2).

The instant claims are drawn to a method of enzymatically processing nucleic acid molecules comprising diluting a mixture of DNA, RNA, degraded or denatured proteins, and a chaotropic agent with an aqueous solution to reduce the concentration of the chaotropic agent to less than 0.01 M and subsequently conducting an enzymatic process, specifically PCR. The enzymatic process occurs without removal of the DNA or RNA from each other or the other components of the mixture.

Regarding claims 1 and 2, Thornhill teaches a method comprising diluting a mixture that includes DNA, RNA, degraded or denatured proteins, and a chaotropic agent with an aqueous reagent to reduce the concentration of the chaotropic agent to less than 0.05 M and subjecting at least some of the DNA and RNA molecules to an enzymatic process without separating them from each other or the other components of the reaction mixture (see page 491).

On page 491, Thornhill teaches lysis of a single cell with the chaotropic agent potassium hydroxide followed by dilution first with neutralization buffer and then with a PCR amplification solution (page 491, column 1). Following the dilution step(s) and without further purification of the diluted mixture (that inherently contains DNA, RNA, degraded or denatured proteins, and the chaotropic agent), Thornhill teaches PCR amplification (page 491, column 2). As evidenced by

the teachings of Builder et al. (see column 9, line 45 – column 10, line 1), potassium hydroxide is a chaotropic agent. Also, the concentration of the chaotropic agent, potassium hydroxide, is reduced to less than 0.05 M in the method of Thornhill. Thornhill teaches use of 5 μl of 200 mM KOH for lysis (page 491, column 1). Upon addition of the sample (1 μl), the neutralization buffer (5 μl), and the PCR amplification mixture (15 μl), the concentration of KOH is reduced to 0.038 mM.

Thornhill also teaches an alternate method where a single cell is lysed with the chaotropic agent SDS (page 491, column 1). As evidenced by Barbeau et al. (US 6,762,160 B2 – see column 9, lines 58-64), SDS is a chaotropic agent. The resulting cell lysate, which contains RNA, DNA, degraded or denatured proteins, and the chaotropic agent, is then diluted with a PCR amplification mixture and used in PCR without further purification of the crude lysate (page 491, columns 1-2). Thornhill teaches that the concentration of SDS is 17 μM. Upon dilution of the 6 μl lysate with 20 μl of the PCR amplification mixture, the concentration of the chaotropic agent is reduced to 4 μM, a concentration less than 0.05 M and less than 0.01 M.

Thus, the teachings of Thornhill anticipate the method of claims 1 and 2.

Regarding claim 3, Thornhill teaches that the mixture includes a cell-lysing detergent (SDS, in the 2nd method), a water-miscible solvent (water), and a neutralizing buffer (200 mM Tricine, in the 1st method), and a reducing agent (50 mM DTT, in the first method) (see page 491, column 1).

Regarding claim 4, Thornhill teaches that dilution is accomplished by serial addition of at least two aqueous reagents (see page 491, where Thornhill teaches dilution first with neutralization buffer and then with the PCR reaction mixture).

Regarding claims 5 and 6, the enzymatic process taught by Thornhill is an exponential amplification method, specifically PCR (page 491, column 2).

Regarding claims 8 and 9, Thornhill teaches that an enzyme for performing the enzymatic process, and specifically a DNA polymerase, is included in the at least one aqueous reagent (see page 491, column 2, where Taq is included in the PCR reaction mixture).

Regarding claims 10 and 11, Thornhill teaches that the dilution and enzymatic process occur in the same container, specifically a tube (page 491).

Regarding claim 12, Thornhill teaches that the mixture is prepared by incubating a sample containing protein-bound RNA and DNA molecules and a chaotropic-agent containing disruption reagent at a concentration of chaotropic agent of at least about 2 M (see page 491, where Thornhill teaches preparing the lysate via incubation with the chaotropic agent SDS or potassium hydroxide). As noted above in section 2, the phrase "at least about 2 M" is completely unclear as to the minimum concentration of chaotropic agent required, and therefore, the teachings of Thornhill anticipate claim 12.

Regarding claim 13, Thornhill teaches that the incubation of the sample and disruption reagent includes heating, whereby the chaotropic agent is concentrated (see page 491, column 1).

Regarding claim 37, Thornhill teaches that incubating and dilution occur in the same container (see page 491).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 14-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thornhill et al. (Prenatal Diagnosis (2001) 21: 490-497) as evidenced by Builder et al. (US 5,407,810) and Barbeau et al. (US 6,762,160 B2) in view of Harvey et al. (US 5,939,259).

Claim 14 is drawn to the method of claim 13, further wherein the heating is sufficient such that the resulting mixture is at least semi-dry. Claim 15 requires this semi-dry mixture is stored prior to use. Claim 16 requires that the heating and subsequent dilution procedure occur in the same container. Claims 17-19 are drawn to the method of claim 12, wherein the disruption reagent is a dry reagent prepared from a water-miscible solvent and an additional component selected from a cell-lysing detergent, a neutralizing buffer, a chelating agent, and a reducing agent.

Thornhill as evidenced by Builder and Barbeau teach the method of claims 1-6, 8-13, and 37, as discussed above.

Regarding claim 14, Thornhill does not teach that the heating step is sufficient to produce a semi-dry mixture.

Regarding claim 15, Thornhill teaches storage of the solution comprising DNA, RNA, degraded or denatured proteins, and a chaotropic agent prior to use (page 491, column 1).

Regarding claim 16, Thornhill teaches that incubation and diluting are carried out in the same container (page 491, column 1).

Regarding claims 17-19, Thornhill does not teach that the disruption reagent is a dry reagent.

Harvey teaches methods and compositions for storage of nucleic acid-containing samples (see abstract). Regarding claims 14, 16, and 17, Harvey teaches spotting a sample containing DNA, RNA, and degraded or denatured proteins onto a surface impregnated with a dry disruption reagent and drying the sample (column 5, lines 10-31). Regarding claim 15, Harvey teaches that this dried sample may be stored prior to use (column 2, lines 46-54). Regarding claim 18, Harvey teaches that the dry disruption reagent is prepared from a mixture that includes a water-miscible solvent (column 5, lines 10-22). Regarding claim 19, Harvey teaches that the disruption reagent may further include a cell-lysing detergent and/or a neutralizing buffer (column 5, lines 1-10).

It would have been prima facie obvious for one of ordinary skill in the art at the time of invention to apply the teachings of Harvey to the method taught by Thornhill. An ordinary practitioner would have recognized that the storage method taught by Harvey, which comprised drying the sample onto a surface impregnated with a dry disruption-reagent, reduced the storage space required for each sample. That is, since Harvey taught storage on one inch squares of

paper (Example 2, column 5, lines 25-55), an ordinary practitioner would have been motivated to substitute this storage method for the method taught by Thornhill, where storage of microcentrifuge tubes was required, in order to maximize the use of the storage space. An ordinary practitioner would have expected a reasonable level of success in applying the teachings of Harvey to the method of Thornhill, since Harvey taught that the dry disruption reagent-impregnated papers were suitable for storage of virtually any nucleic acid-containing sample (see abstract and column 3, lines 6-14). Thus, an ordinary practitioner of the method taught by Thornhill would have been motivated to dry the samples on a surface impregnated with a disruption reagent, as suggested by Harvey, thereby resulting in the instantly claimed methods.

8. Claims 17-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thornhill et al. (Prenatal Diagnosis (2001) 21: 490-497) as evidenced by Builder et al. (US 5,407,810) and Barbeau et al. (US 6,762,160 B2) in view of Pourahmadi et al. (US 6,440,725 B1; cited previously).

The instant claims 17-21 are drawn to the method of claim 12, further wherein the disruption reagent is a dry disruption reagent prepared from a mixture that includes a water-miscible solvent and an additional component selected from a cell-lysing detergent, a neutralizing buffer, a chelating agent, and a reducing agent. This dry disruption reagent is adhered to a surface of the container. Claim 22 is drawn to the method of claim 20, wherein the sample comprises from a fraction of a cell up to 200 cells. Claim 23 is drawn to the method of claim 22, wherein the amount of disruption reagent is sufficient to provide a 2-8 M concentration of the chaotropic agent in a volume of 20-50 nl.

Thornhill as evidenced by Builder and Barbeau teach the method of claims 1-6, 8-13, and 37, as discussed above.

Regarding claim 22, Thornhill teaches that the sample is a single cell (page 491, column 1).

Regarding claim 23, the amount of disruption reagent taught by Thornhill is sufficient to provide a concentration of 10 M of the chaotropic agent in a volume of 20-50 nl, rather than the instantly claimed range of 2-8 M. Thornhill teaches that the disruption reagent is 5 μl of 200 mM KOH (page 491, column 1). The molecular weight of KOH is 56.10564 g/mol. Therefore, the 5 μl of KOH taught by Thornhill contains 0.000011221128 g of KOH. Resuspension of this amount of KOH in 20 nl results in a 10 M solution of KOH.

Regarding claims 17-21, Thornhill does not teach that the disruption reagent is a dry reagent adhered to a surface of the tube.

Pourahmadi teaches methods for nucleic acid purification and amplification in an integrated microfluidic cartridge (see abstract, column 2, lines 25-45, column 3, lines 22-42, and column 5, lines 11-24 for a general description). Regarding claims 17-21, Pourahmadi teaches cell lysis using a dried disruption reagent coated on a surface within the cartridge (column 12, lines 34-50). Pourahmadi teaches that the dried disruption reagent may be prepared from a mixture that includes a water-miscible solvent, cell-lysing detergents, buffers, and enzymes (column 12, lines 21-29 and column 16, lines 22-39). Finally, Pourahmadi teaches that, "Reagents containing compounds that are thermally unstable when in solution can be stabilized by drying using common techniques such as lyophilization (column 12, lines 54-57)."

It would have been prima facie obvious for one of ordinary skill in the art at the time of invention to coat a surface of the tubes taught by Thornhill with a dried version of the disruption reagent. An ordinary practitioner would have been motivated to do so, since Pourahmadi taught that the stability of thermally unstable reagents, such as proteinase K, could be improved by drying (column 12, lines 54-57. An ordinary practitioner would have recognized that improving the stability of the proteinase K-based disruption reagent would carry the advantage of reducing false negative amplification results stemming from an absence of target DNA due to incomplete lysis by inactive or degraded proteinase K. Since Pourahmadi expressly suggested drying enzymes (column 12, lines 21-29), an ordinary practitioner would have expected a reasonable level of success in drying the proteinase K taught in the method of Thornhill. Therefore, the methods of the instant claims 17-22 are prima facie obvious in view of the teachings of Thornhill as evidenced by Barbeau and Builder in combination with the teachings of Pourahmadi.

Regarding claim 23, it would have been prima facie obvious for one of ordinary skill in the art at the time of invention to optimize the amount of disruption reagent used in the method resulting from the teachings of Thornhill as evidenced by Builder and Barbeau in combination with Pourahmadi. As noted above, Thornhill taught an amount of disruption reagent highly similar to the claimed amount. Specifically, the amount of disruption reagent taught by Thornhill is sufficient to give a concentration of chaotropic agent of 10 M in 20 nl, rather than the instantly claimed concentration of 2-8 M. An ordinary practitioner would have recognized that this results-effective variable could be optimized in order to achieve the desired results. For example, an ordinary practitioner would have been motivated to optimize the amount of disruption reagent to achieve efficient lysis using the minimum concentration of chaotropic

agent, thereby conserving valuable reagents. As noted in MPEP 2144.05 II A, "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. '[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.' In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)." Routine optimization is not inventive, and no evidence has been presented to suggest that the selection of the claimed amounts of disruption reagent was other than routine or that the results should be considered unexpected over the closest prior art. Therefore, in the absence of secondary considerations, the method of claim 23 is prima facie obvious over Thornhill as evidenced by Builder and Barbeau in view of Pourahmadi.

9. Claim 38 is rejected under 35 U.S.C. 103(a) as being unpatentable over Thornhill et al. (Prenatal Diagnosis (2001) 21: 490-497) as evidenced by Builder et al. (US 5,407,810) and Barbeau et al. (US 6,762,160 B2).

Claim 38 is drawn to the method of claim 12, further wherein the amount of disruption reagent is sufficient to provide a 2-8 M concentration of the chaotropic agent in a volume of 20-50 nl.

Thornhill as evidenced by Builder and Barbeau teaches the method of claims 1-6, 8-13, and 37, as discussed above.

Regarding claim 38, the amount of disruption reagent taught by Thornhill is sufficient to provide a concentration of 10 M of the chaotropic agent in a volume of 20-50 nl, rather than the

instantly claimed range of 2-8 M. Thornhill teaches that the disruption reagent is 5 µl of 200 mM KOH (page 491, column 1). The molecular weight of KOH is 56.10564 g/mol. Therefore, the 5 µl of KOH taught by Thornhill contains 0.000011221128 g of KOH. This amount of KOH in 20 nl is a 10 M solution.

It would have been prima facie obvious for one of ordinary skill in the art at the time of invention to optimize the amount of disruption reagent used in the method of Thornhill. As noted above, Thornhill teaches an amount of disruption reagent highly similar to the claimed amount. Specifically, the amount of disruption reagent taught by Thornhill is sufficient to give a concentration of chaotropic agent of 10 M in 20 nl, rather than the instantly claimed concentration of 2-8 M. An ordinary practitioner would have recognized that this results-effective variable could be optimized in order to achieve the desired results. For example, an ordinary practitioner would have been motivated to optimize the amount of disruption reagent to achieve efficient lysis using the minimum concentration of chaotropic agent, thereby conserving valuable reagents. As noted in MPEP 2144.05 II A, "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. '[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.' In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)." Routine optimization is not inventive, and no evidence has been presented to suggest that the selection of the claimed amounts of disruption reagent was other than routine or that the results should be considered unexpected over the closest prior art.

Therefore, in the absence of secondary considerations, the method of claim 38 is prima facie obvious over Thornhill as evidenced by Builder and Barbeau.

Conclusion

10. No claims are currently allowable.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Ryder et al. (US 5,639,599) and Tsai (Prenatal Diagnosis (1999) 19: 1048-1051) teach nucleic acid amplification using crude cell lysates prepared using chaotropic agents that have not been further purified prior to the amplification step (see Example 1, columns 11-13, of Ryder and page 1049, column 2 of Tsai). Kappel et al. (US 2004/0259162 A1) teach a container coated with a dried lysis reagent for nucleic acid purification (see paragraphs 103-106 116-118, and 120).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Angela Bertagna whose telephone number is 571-272-8291. The examiner can normally be reached on M-F, 7:30 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Angela Bertagna
Art Unit 1637
April 27, 2007

amb

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
4/30/07